to less than 100% per 6 months and/or at least one microbicide in an amount that reduces the bacterial count of 1 million germs added per gram of total mass of the formulation to less than 100 in the case of aerobic bacteria, to less than 10 in the case of entero-bacteria, and to less than 1 in the case of Pseudomonas aeruginosa or Staphilococcus aureus, after a period of 4 days. --

In the Claims:

Please cancel claims 8, 10, 15-20, 25, 42 and 43 without prejudice.

Please amend claims 1-7, 9, 11-14, 21-24, 26-41 and 44-50 as follows:

1. (Amended) A formulation comprising penetrants being capable of penetrating the pores of a barrier, even when the average diameter of said pores is smaller than the average diameter of said penetrants, wherein said penetrants can transport agents or enable agent penetration through said pores after said penetrants have entered said pores, wherein the formulation comprises

at least one consistency builder in an amount that increases the formulation viscosity above that of the non-thickened corresponding formulation to maximally 5 Ns/m^2 so that spreading over, and retention at, the application area is enabled, or

at least one antioxidant in an amount that reduces the increase of oxidation index to less than 100 % per 6 months, or

at least one microbicide in an amount that reduces the bacterial count of 1 million germs added per gram of total mass of the formulation to less than 100 in the case of aerobic bacteria, to less than 10 in the case of entero-bacteria, and to less than 1 in the case of Pseudomonas aeruginosa or Staphilococcus aureus, after a period of 4 days.

2. (Amended) The formulation according to claim 1, wherein said at least one consistency builder is added in an amount that increases the formulation viscosity to up to 1 Ns/m^2.

3. (Amended) The formulation according to claim 1, wherein said at least one antioxidant is added in an amount that reduces the increase of oxidation index to less than 100 % per 12 months.

4. (Amended) The formulation according to claim 1, wherein said at least one microbicide is added in an amount that reduces the bacterial count of 1 million germs added per gram of total mass of the formulation to less than 100 in the case of aerobic bacteria, to less than 10 in the case of entero-bacteria, and to less than 1 in the case of Pseudomonas aeruginosa or Staphilococcus aureus, after a period of 3 days.

5. (Amended) The formulation according to claim 1, wherein the consistency builder is selected from the group consisting of:

pharmaceutically acceptable hydrophilic polymers, including partially etherified cellulose derivatives, comprising carboxymethyl -, hydroxyethyl-, hydroxypropyl-, hydroxypropylmethyl- or methyl-cellulose;

completely synthetic hydrophilic polymers including polyacrylates, polymethacrylates, poly(hydroxyethyl)-, poly(hydroxypropyl)-, poly(hydroxypropylmethyl)methacrylate, polyacrylonitrile, methallyl-sulphonate, polyethylenes, polyoxiethylenes, polyethylene glycols, polyethylene glycol-lactide, polyethylene glycol-diacrylate, polyvinylpyrrolidone, polyvinyl alcohols, poly(propylmethacrylamide), poly(propylene fumarate-co-ethylene glycol), poloxamers, polyaspartamide, (hydrazine cross-linked) hyaluronic acid, silicone;

natural gums including alginates, carrageenan, guar-gum, gelatine, tragacanth, (amidated) pectin, xanthan, chitosan collagen, agarose; and

mixtures and further derivatives or co-polymers thereof.

6. (Amended) The formulation according to claim 5, wherein the polymer weight fractions are in the range between 0.05 % and 10%.

7. (Amended) The formulation according to claim 1, wherein the anti-oxidant is selected from the group consisting of:

synthetic phenolic antioxidants, including butylated hydroxyanisol (BHA), butylated hydroxytoluene (BHT) and di-tert-butylphenol (LY178002, LY256548, HWA-131, BF-389, CI-986, PD-127443, E-5119, BI-L-239XX), tertiary butylhydroquinone (TBHQ), propyl gallate (PG), 1-O-hexyl-2,3,5-trimethylhydroquinone (HTHQ);

aromatic amines, including diphenylamine, p-alkylthio-o-anisidine, ethylenediamine derivatives, carbazol and tetrahydroindenoindol;

phenols and phenolic acids, including guaiacol, hydroquinone, vanillin, gallic acids and their esters, protocatechuic acid, quinic acid, syringic acid, ellagic acid, salicylic acid, nordihydroguaiaretic acid (NDGA), eugenol;

tocopherols and their derivatives including tocopheryl-acylate, -laurate, myristate, -palmitate, -oleate,-linoleate, or any other suitable tocopheryl-lipoate, tocopheryl-POE-succinate;

trolox and corresponding amide and thiocarboxamide analogues;

ascorbic acid and its salts, isoascorbate, (2 or 3 or 6)-o-alkylascorbic acids, ascorbyl esters, including 6-o-lauroyl, myristoyl, palmitoyl-, oleoyl, or linoleoyl-L-ascorbic acid;

non-steroidal anti-inflammatory agents (NSAIDs), such as indomethacine, diclofenac, mefenamic acid, flufenamic acid, phenylbutazone, oxyphenbutazone acetylsalicylic acid, naproxen, diflunisal, ibuprofene, ketoprofene, piroxicam, penicillamine, penicillamine disulphide, primaquine, quinacrine, chloroquine, hydroxychloroquine, azathioprine, phenobarbital, acetaminephen;

aminosalicylic acids and derivatives;

methotrexate, probucol, antiarrhythmics, including amiodarone, aprindine, asocainol;

ambroxol, tamoxifene, b-hydroxytamoxifene;

calcium antagonists, including nifedipine, nisoldipine, nimodipine, nicardipine, nilvadipine, beta-receptor blockers including atenolol, propranolol and nebivolol;

sodium bisulphite, sodium metabisulphite, thiourea;

chellating agents, including EDTA, GDTA, desferral;

miscellaneous endogenous defence systems, including transferrin, lactoferrin, ferritin, cearuloplasmin, haptoglobion, haemopexin, albumin, glucose, ubiquinol-10;

enzymatic antioxidants, including superoxide dismutase and metal complexes with a similar activity, including catalase, glutathione peroxidase, and less complex molecules, including beta-carotene, bilirubin, uric acid;

flavonoids including flavones, flavonols, flavonones, flavanonals and chacones, anthocyanins;

N-acetylcystein, mesna, glutathione, thiohistidine derivatives, triazoles;

tannines, cinnamic acid, hydroxycinnamatic acids and their esters, including coumaric acids and esters, caffeic acid and their esters, ferulic acid, (iso-) chlorogenic acid, sinapic acid;

spice extracts, including spice extracts from clove, cinnamon, sage, rosemary, mace, oregano, allspice and nutmeg;

carnosic acid, carnosol, carsolic acid; rosmarinic acid, rosmaridiphenol, gentisic acid, ferulic acid;

oat flour extracts, including avenanthramide 1 and 2; thioethers, dithioethers, sulphoxides, tetralkylthiuram disulphides;

phytic acid, steroid derivatives, including U74006F; and

tryptophan metabolites, including 3-hydroxykynurenine and 3-hydroxyanthranilic acid, and organochalcogenides.

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9. (Amended) The formulation according to claim 1, wherein the microbicide is selected from the group consisting of:

short chain alcohols, including ethyl and isopropyl alcohol, chlorbutanol, benzyl alcohol, chlorbenzyl alcohol, dichlorbenzylalcohol, hexachlorophene;

phenolic compounds, including cresol, 4-chloro-m-cresol, p-chloro-m-xylenol, dichlorophene, hexachlorophene, povidon-iodine;

parabenes, including alkyl-parabenes, including methyl-, ethyl-, propyl-, or butyl-paraben, benzyl paraben;

acids, including sorbic acid, benzoic acid and their salts;

quaternary ammonium compounds, including alkonium salts, benzalkonium salts, including a chloride or a bromide, cetrimonium salts, phenoalkecinium salts, including phenododecinium bromide, cetylpyridinium chloride and other salts;

mercurial compounds, including phenylmercuric acetate, borate, or nitrate, thiomersal, chlorhexidine or its gluconate, and mixtures thereof.

11. (Amended) The formulation comprising penetrants being capable of penetrating the pores of a barrier, even when the average diameter of said pores is smaller than the average diameter of said penetrants, wherein said penetrants can transport agents or enable agent penetration through said pores after said penetrants have entered said pores, the agents associated with said penetrants being corticosteroids, especially glucocorticoids or mineralocorticosteroids, wherein the relative content of corticosteroids is above 0.1 weight-%, relative to total dry mass of the formulation.

12. (Amended) The formulation according to claim 11, further comprising at least one consistency builder or at least one anti-oxidant or at least one microbicide and mixtures thereof.

13. (Amended) The formulation according to claim 11, wherein the corticosteroid is selected from the group consisting of: alclonetasone dipropionate, amcinonide, beclomethasone dipropionate, betamethasone, betamethasone 17-valerate, betamethasone 17,21-divalerate, betamethasone 21-acetate, betamethasone 21-buytrate, betamethasone 21-propionate, betamethasone 21-valerate, betamethasone benzoate, betamethasone dipropionate, betamethasone valerate, budesonide, clobetasol propionate, clobetasone butyrate, cortexolone, corticosterone, cortisone, cortisone 17-acetate, 21-deoxybetamethasone, 21-deoxybetamethasone 17-propionate, deoxycorticosterone, desonide, desoxymethasone, dexamethasone, diflorasone diacetate, diflucortolone valerate, fluclorolone acetonide, flumethasone pivalate, fluocinolone acetonide, fluocinonide, fluocortin butyl, fluocortolone , 9-alpha-fluorocortisone, 9-alpha-fluorohydrocortisone, 9-alpha-fluoroprednisolone, fluprednidene acetate, flurandrenolone,

halcinonide, hydrocortisone, hydrocortisone 17-acetate, hydrocortisone 17-butyrate, hydrocortisone 17-propionate, hydro cortisone 17-valerate, hydrocortisone 21-acetate, hydrocortisone 21-butyrate, hydrocortisone 21-propionate, hydrocortisone 21-valerate, 17-alpha-hydroxyprogesterone, methylprednisolone acetate, mometasone furoate, prednisolone, prednisone, prednisone 17-acetate, prednisone 17-valerate, progesterone, triamcinolone, and triamcinolone acetonide.

14. (Amended) The formulation according to claim 1, wherein the penetrants are suspended or dispersed in a polar liquid in the form of fluid droplets surrounded by a membrane-like coating of one or several layers, said coating comprising at least two kinds or forms of amphiphilic substances with a tendency to aggregate,

wherein said at least two substances differ by at least a factor of 10 in solubility in said liquid or wherein said substances when in the form of homo-aggregates, for the more soluble substance, or of hetero-aggregates, for any combination of both said substances, have a preferred average diameter smaller than the diameter of the homo-aggregates containing merely the less soluble substance; or

wherein the presence of the more soluble substance lowers the average elastic energy of the membrane-like coating in the vicinity of thermal energy.

21. (Amended) The formulation according to claim 14, wherein the average penetrant diameter is between 30 nm and 500 nm.

22. (Amended) The formulation according to claim 14, wherein the average diameter of the penetrant is 2 to 25 times bigger than the average diameter of the pores in the barrier.

23. (Amended) The formulation according to claim 14, wherein the dry weight of all carrier droplets in a formulation for the use on human or animal skin is 0.01 weight-% (w-%) to 40 w-% of total formulation mass.

24. (Amended) The formulation according to claim 14, wherein the dry weight of all carrier droplets in a formulation for the use on human or animal mucosa is 0.0001 w-% to 30 w-% of total formulation mass.

26. (Amended) A method for preparing a formulation for non-invasive application in vivo, according to claim 11, comprising forming penetrants capable of associating or incorporating said agent molecules from at least one amphiphilic substance, at least one polar fluid, at least one edge-active substance or surfactant, at least one corticosteroid in an amount of more than 0.1 w-% based on total dry mass of the formulation, and other pharmaceutically acceptable ingredients.

27. (Amended) The method of claim 26, wherein at least one edge-active substance or surfactant, at least one amphiphilic substance, at least one hydrophilic fluid and the agent are dissolved to form a solution and optionally are mixed separately, the resulting (partial) mixtures or solutions then being combined to subsequently induce, preferably by action of mechanical energy including shaking, stirring, vibrating, homogenising, ultrasonication, shear, freezing and thawing, or filtration using convenient driving pressure, the formation of penetrants that associate with or incorporate the agent.

28. (Amended) The method of claim 26, wherein said amphiphilic substances are either used as such, or dissolved in a physiologically compatible polar fluid, which may be water or miscible with water, or in a solvation-mediating agent, together with a polar solution.

29. (Amended) The method of claim 26, wherein said amphiphilic substances are dissolved in highly volatile alcohols or in pharmaceutically acceptable organic solvents, which are then removed prior to making final preparation.

30. (Amended) The method as claimed in claim 26, wherein the polar solution contains at least one edge-active substance or surfactant.

31. (Amended) The method according to claim 26, wherein the formation of said penetrants is induced by the addition of required substances into a fluid phase, evaporation from a reverse phase, by injection or dialysis, if necessary under the influence of mechanical stress, including shaking, stirring, vibrating, homogenising, ultrasonication, shearing, freezing and thawing, or filtration using low (1 MPa) or intermediate (up to 10 MPa) driving pressure.

32. (Amended) The method of claim 31, wherein the formation of said penetrants is induced by filtration, the filtering material having pores sizes between 0.01 μm and 0.8 μm.

33. (Amended) The method according to claim 26, further comprising associating said agents and penetrants, at least partly, after the formation of said penetrants, by injecting a solution of the drug in a pharmaceutically acceptable fluid, including ethanol, 1-and 2-propanol, benzyl alcohol, propylene glycol, polyethylene glycol (molecular weight: 200 – 400 D) or glycerol, into the suspending medium, wherein said penetrants being formed previously, using the corresponding or some other suitable manufacturing method, or simultaneously with the drug injection, if required using a co-solution of the drug and, at least some, penetrant ingredients.

34. (Amended) The method according to claim 26, wherein said penetrants, with which the agent molecules are associated or into which the agent is incorporated, are prepared just before the application of the formulation, if convenient from a suitable concentrate or a lyophylisate.

35. (Amended) The formulation according to claim 11, wherein the content of corticosteroids is between 0.1 w-% and 20 w-%.

36. (Amended) The formulation according to claim 35, wherein the relative content of corticosteroids in the case of triamcinolone or one of its derivatives, such as acetonide, is below 2 w-%, relative to total dry mass of the drug-loaded carriers.

37. (Amended) The formulation according to claim 36, wherein the relative content of corticosteroids in the case of hydrocortisone or one of its derivatives is below 20 w-%, relative to total dry mass of the drug-loaded carriers.

38. (Amended) The formulation according to claim 35, wherein the relative content of corticosteroids in the case of dexamethasone or one of its derivatives is below 15 w-%, relative to total dry mass of the drug-loaded carriers.

39. (Amended) The formulation according to claim 35, wherein the relative content of corticosteroids in the case of clobetasol or one of its derivatives, such as propionate is below 15 w-%, relative to total dry mass of the drug-loaded carriers.

40. (Amended) The formulation according to claim 35, wherein the content of said corticosteroid is below the saturation maximum, defined as the content of corticosteroid at which the corticosteroid begins to crystallise in or outside the carrier.

41. (Amended) The formulation according to claim 1, wherein in order to speed up drug action a permeation enhancer is added.

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44. (Amended) The formulation according to claim 11, wherein said corticosteroid is added in an amount which enables the formulation to be applied corresponding to an area dose, as expressed by the total dry mass of penetrant applied per unit area, of between 0.1 mg cm^{-2} and 15 mg cm^{-2}, if said corticosteroid is desired to exert a therapeutic effect in the deep subcutaneous tissue or the remote tissues, including the whole body.

45. (Amended) The formulation according to claim 11, wherein said corticosteroid is added in an amount which enables the formulation to be applied with an area dose, as expressed by the total dry mass of penetrant applied per unit area, of between 1 $\mu g\ cm^{-2}$ and 250 $\mu g\ cm^{-2}$, if said corticosteroid is desired to exert a mainly local rather than systemic therapeutic effect.

46. (Amended) The formulation according to claim 11, wherein consistency and, if necessary other characteristics of the formulation are appropriately selected to enable spraying, smearing, rolling or sponging of the formulation on the application area in particular by using a sprayer, spender, roller or sponge.

47. (Amended) A method for non-invasive application of corticosteroids by means of penetrants according to claim 1, wherein the area dose, as expressed by the total dry mass of penetrant applied per unit area, is selected to be between 0.1 $mg\ cm^{-2}$ and 15 $mg\ cm^{-2}$, if said corticosteroid is desired to exert a therapeutic effect in the deep subcutaneous tissue or the remote tissues, including the whole body.

48. (Amended) A method for non-invasive application of corticosteroids by means of penetrants according to claim 1, wherein the area-dose, as expressed by the total dry mass of penetrants applied per unit area, is between 1 $\mu g\ cm^{-2}$ and 250 $\mu g\ cm^{-2}$, if said corticosteroid is desired to exert a mainly local rather than systemic therapeutic effect.

49. (Amended) A method for non-invasive application of corticosteroids associated with or encapsulated into said penetrants according to claim 1, wherein the formulation is applied by spraying, smearing, rolling or sponging on the application area in particular by using a sprayer, spender, roller or sponge.

50. (Amended) Use of a formulation in accordance with claim 1 for the treatment of inflammatory disease, dermatosis, kidney or liver failure, adrenal insufficiency, aspiration